

Comparison of intermittent haemodialysis, prolonged intermittent renal replacement therapy and continuous renal replacement haemofiltration for lithium toxicity: a case report

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Clinical record

A 51-year-old man who weighed 90 kg presented to our emergency department (ED) 7 hours after a suicide attempt. He had ingested 343 lithium carbonate tablets (250 mg each; total 85.75 g, 2300 mmol), 49 olanzapine tablets (10 mg each; 490 mg) and had inhaled natural gas by turning on his gas cooking unit. He was known to suffer from paranoid schizophrenia and was prescribed lithium carbonate and olanzapine for this condition. He also had a significant smoking history.

At presentation, his Glasgow Coma Scale score was 14 with no focal neurological signs. He passed 4 L of watery stool secondary to lithium overdose in the first 2 hours of admission. His urine output was adequate, and he had an elevated creatinine level on admission (155 $\mu\text{mol/L}$; reference range, 60–110 $\mu\text{mol/L}$).

Laboratory investigations revealed a markedly elevated plasma lithium level of 9.6 mmol/L (therapeutic range, 0.6–1.2 mmol/L), which increased to 13.2 mmol/L within 2 hours. The patient's arterial carboxyhaemoglobin level was 3.6% (reference range for smokers, 1%–15%).¹ Given his history of smoking, the natural gas poisoning was thought to be insignificant.

The patient was fluid resuscitated with 8 L of 0.9% saline over 4 hours due to 4 L of diarrhoea. Charcoal was not administered as it does not bind to lithium. Three hours after presentation, he became progressively more agitated and required endotracheal intubation so that ongoing treatment and dialysis could be administered safely. A central venous catheter and right internal jugular dialysis access catheter were inserted while the patient was still in the ED.

The patient was subsequently transferred to our intensive care unit. Urgent dialysis was started in the ICU. The first session of intermittent haemodialysis (IHD) was started 12 hours post lithium ingestion (PLI) using an AK 200 S dialysis machine (Gambro, Sydney, NSW). IHD was chosen because it is widely recognised as the most efficient means of plasma lithium removal.² After 4 hours of treatment with IHD (12–16 hours PLI), his plasma lithium level fell to 4.7 mmol/L. However, it was expected to rise over the next few hours due to rebound phenomenon. As IHD was not available overnight in our ICU, prolonged intermittent renal replacement therapy (PIRRT) using a 4008S ARtplus dialysis machine (Fresenius

ABSTRACT

This case report compares three types of renal replacement therapy for acute severe lithium toxicity and is the first to use prolonged intermittent renal replacement therapy (PIRRT). A peak lithium level of 13.2 mmol/L was recorded after a 51-year-old man attempted suicide. He was treated with intermittent haemodialysis (IHD), PIRRT and continuous venovenous haemofiltration (CVVH) over 55 hours. Lithium clearance was shown to be comparable between IHD and PIRRT, both of which were superior to CVVH. Expected efficacy of treatment with a single daily session of PIRRT was higher than IHD or CVVH. PIRRT is a useful strategy for dialysis among patients with acute lithium intoxication.

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Medical Care Australia, Sydney, NSW) was started. Due to technical issues, initiation of PIRRT was delayed by 6 hours. His plasma lithium level rebounded to 7.5 mmol/L during this time. Once commenced, PIRRT was used for 4 hours (22–26 hours PLI) before IHD became available again in the morning.

A second 4-hour IHD session was employed thereafter (28–32 hours PLI). The patient's plasma lithium level was 2.4 mmol/L at the end of the second IHD session, and it increased to 5.1 mmol/L within 4 hours of ceasing renal replacement therapy (36 hours PLI). Due to technical issues with our PIRRT machine, the patient was then treated with an 8-hour session of continuous venovenous haemofiltration (CVVH) using a 45 mL/kg/h substitution rate (38–46 hours PLI, Prismaflex machine with software version 5.0 installed [Gambro, Sydney, NSW]). A further 3-hour session of IHD was performed on Day 3, after which dialysis was no longer needed. Figure 1 shows the timeline of dialysis and corresponding plasma lithium level during and between dialysis sessions.

The timing of each modality of dialysis along with blood flow rate and dialysate and/or substitution rate is shown in Table 1. Also shown are the pre- and postfilter plasma lithium levels that were measured in all modalities.

The patient developed septic shock on Day 3 of ICU admission. Vasopressors were required for 48 hours (noradrenaline, peak dose 0.2 $\mu\text{g/kg/min}$) and antibiotics were given (piperacillin–tazobactam 4.5 g three times a day and

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vancomycin 1 g twice a day). No source of sepsis could be identified. The patient was successfully extubated on Day 5. On Days 6 and 7 the patient was ataxic and tremulous, which was presumed due to lithium encephalopathy. This settled by Day 9 and the patient was discharged to the hospital's psychiatric services.

Discussion

We report a patient who was taking lithium who presented after acute ingestion of 85.75 g of lithium. His peak lithium plasma level was 13.2 mmol/L. Lithium is widely distributed in total body water. It has a small volume of distribution 0.6–0.9 L/kg bodyweight with no protein binding and is cleared

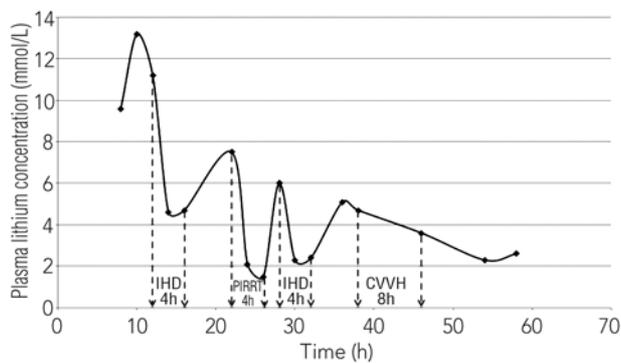
primarily by the kidneys. It is therefore suited for extracorporeal elimination. It is recommended that patients who have lithium level greater than 4 mEq/L with altered mental status due to acute toxicity should be considered for dialysis.³ Among patients with normal renal function, the clearance rate is 25–35 mL/min.⁴

For our patient's treatment, we used IHD, PIRRT and CVVH. IHD was used because it is thought to be the most efficient way of rapidly removing lithium. We believed PIRRT would perform better than CVVH because it has higher dialysate and substitution flow rates than CVVH. CVVH was employed as a substitute for PIRRT because of technical issues with our PIRRT machine. However, use of all three modalities allowed us to compare the clearance and expected efficacy of full treatment with each modality.

IHD has a high clearance for lithium and the plasma lithium level therefore rapidly drops. However, because lithium is distributed in the intracellular compartment, the lithium level rebounds within a few hours. Multiple sessions of IHD may be required for managing lithium toxicity.⁵

PIRRT is also known as sustained low-efficiency daily dialysis (SLEDD-f). It is a hybrid modality in which solute is cleared by diafiltration. It can be operated by ICU nursing staff and therefore does not require the services of the dialysis unit to run it. It operates for longer treatment sessions (up to 10 hours with our machine) with lower blood and dialysate flow rates than IHD⁶ but higher rates than CVVH. In PIRRT, dialysate and substitution fluid are produced from tap water using an on-line reverse osmosis unit and ultra filters to achieve bacteria- and pyrogen-free fluid to which concentrate is added. This is contrasted with the use of industrially

Figure 1. Change in plasma lithium concentration over time



IHD = intermittent haemodialysis. PIRRT = prolonged intermittent renal replacement therapy. CVVH = continuous venovenous haemofiltration.

Table 1. Extraction ratio, clearance and expected efficacy of full treatment of lithium toxicity for three dialysis modalities, based on our patient's outcomes

Time PLI, h	Dialysis modality	Haematocrit	BFR, mL/h	DR or SR, mL/h	Pa, mmol/L	Pv, mmol/L	ER	K, mL/min	Expected efficacy, Kt/V
12	IHD	0.48	300	DR 700	11.2	0.5	0.96	150	0.67
14			300	DR 700	4.6	<0.2	0.96	150	
16			300	DR 700	4.7	<0.2	0.96	150	
22	PIRRT	0.48	300	DR 300; SR 100	7.5	<0.2	0.97	152	1.35
24			300	DR 300; SR 100	2.1	<0.2	0.91	142	
26			300	DR 300; SR 100	1.5	<0.2	0.87	137	
28	IHD		350	DR 700	6.0	<0.2	0.97	178	0.79
30			350	DR 700	2.3	<0.2	0.91	167	
32			350	DR 700	2.4	<0.2	0.92	169	
38	CVVH	0.37	300	SR 67	4.7	3.1	0.34	64	1.02
46			250	SR 67	3.6	2.2	0.32	61	

PLI = post lithium ingestion. BFR = blood flow rate. DR = dialysate rate. SR = substitution rate. Pa = plasma lithium concentration from arterial (afferent) limb. Pv = plasma lithium concentration from venous (efferent) limb. ER = extraction ratio. K = instantaneous clearance. t = duration of dialysis in minutes. V = volume of distribution of lithium in mL, based on 0.75 L/kg bodyweight. IHD = intermittent haemodialysis. PIRRT = prolonged intermittent renal replacement therapy. CVVH = continuous venovenous haemofiltration.

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prepared bags of dialysate fluid with CVVH. On-line production may result in cost saving, depending on how often the treatment is used in the hospital unit.

The clearance rate of CVVH is lower than that of IHD. This results from lower blood flow rate and lower dialysate or substitution rate (depending on whether continuous venovenous haemodialysis or CVVH are used, respectively). Longer durations of treatment, compared with IHD, may compensate for the lower clearance and achieve similar efficacy and solute clearance.⁷

We calculated the extraction ratio, clearance and expected efficacy of full treatment for lithium removal (see Table 1 for data and derived units) according to the formulae

$$\text{Extraction ratio} = \frac{P_a - P_v}{P_a}$$

$$\text{Plasma flow rate} = \text{blood flow rate} \times (1 - \text{haematocrit})$$

$$K = \text{extraction ratio} \times \text{plasma flow rate}$$

$$\text{Expected efficacy} = \frac{(K \times t)}{V} \quad (\text{using clearance at dialysis initiation})$$

Where P_a is the plasma lithium concentration from an arterial (afferent) limb; P_v is the plasma lithium concentration from venous (efferent) limb; K is the instantaneous clearance at dialysis initiation; t is the duration of dialysis; and V is the volume of distribution of lithium.

The extraction ratio was over 85% for IHD and PIRRT but only 34% for CVVH despite using a 45 mL/kg/h substitution rate. Instantaneous clearance was similar in IHD and PIRRT but lower for CVVH.

The calculated efficacy is an "expected" value in this case because it is based on the assumption that the patient received the full duration of treatment. We assumed the full duration of treatment per daily session to be 5 hours for IHD, 10 hours for PIRRT and 18 hours for CVVH. For the purpose of calculation, instantaneous clearance at the start of each dialysis modality was used. As the concentration of solute decreases over time, the instantaneous clearance also drops. The expected efficacy is therefore overestimated in the calculation for all three dialysis modalities. Lithium is assumed to have a volume of distribution of 0.75 L/kg bodyweight for this 90 kg patient.

As shown in Table 1, instantaneous clearance is comparable between IHD and PIRRT. Instantaneous clearance for CVVH is almost half that of other techniques. However, if expected efficacy is calculated for the full treatment duration each day (5 hours for IHD, 10 hours for PIRRT and 18 hours for CVVH), PIRRT achieved highest efficacy (1.35), CVVH had intermediate efficacy (1.02), and IHD had the lowest efficacy (0.67 and 0.79).

We used plasma lithium concentrations for our calculations as we are unable to obtain whole blood lithium measurement in our laboratory. Red blood cell concentration of lithium may correlate closely with brain concentrations. A study by Camus and colleagues measured lithium concentrations in red blood

cells and plasma of 49 patients.⁸ They found in acute toxicity the red cell to plasma lithium concentration ratio was 0.48. After dialysis, plasma lithium concentrations were rapidly reduced but red cell lithium levels were reduced to a lesser extent.⁸

We are not aware of any reports of use of PIRRT for lithium toxicity, but its use for a patient with sodium valproate overdose has been documented previously.⁹ Our patient's outcomes suggest that for acute lithium toxicity, PIRRT is highly efficacious. It can achieve higher efficacy than IHD or CVVH. Because it can be run without the help of the dialysis services, like CVVH in most units, it offers more flexibility in timing, duration and frequency of treatment. Its use in toxicity of chemicals cleared by dialysis deserves further evaluation.

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